U.S. Patent Application Serial No. 10/560,790   Conf. No. 4918
Amendment and Response dated June 3, 2009
Reply to Office Action of January 7, 2009

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1-28 (Cancelled)

29. (Currently Amended) A composition for treating or preventing arthritis or other degenerative disease, said composition comprising one or more polypeptides fragment having at least 65% amino acid identity to SEQ ID NO: 14 and having an amino acid length of less than 250 amino acids, in combination with a physiological acceptable carrier, wherein said polypeptide fragment induces tolerance to cartilage, and wherein the polypeptide comprises one or more polypeptide fragments selected from:

                    (a) KSVSFSYKG (SEQ ID NO: 2);
                    (b) QSVVFSYKG (SEQ ID NO:20)
                    (c) KIMIGVERS (SEQ ID NO: 3);
                    (d) RIESLPIKPRG (SEQ ID NO: 5);
                    (e) KHWSIWQIQDSSGKE (SEQ ID NO: 6);
                    (f) KNWNIWQIQDSSGKE (SEQ ID NO:21)
                    (g) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);
                    (h) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)
                    (i) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);
                    (j) RNLYPSGLPEEYSFLTTFRM (SEQ ID NO:23);
                    (k) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);
                    (l) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and
                    (m) RSSATLFVDCNRI [SEQ ID NO: 11].

30. (Currently Amended) The composition of claim 29, wherein the polypeptide fragment has a molecular weight of:

          a) less than 30,000 Da, or

          b) less than 30,000 Da and greater than or equal to 10,000 Da.

31. (cancelled)

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32. (Currently Amended) The composition of claim 29, wherein the polypeptide ~~fragment~~ has identity to SEQ ID NO: 14 that is:

      a) at least 80%;

      b) at least 90%; or

      c) 100%.

33.-34. (cancelled)

35. (withdrawn) A method of inducing tolerance to at least one antigenic component of cartilage in an individual, the method comprising administering to the individual the composition of claim 29, wherein said administering induces said tolerance.

36. (withdrawn) The method of claim 35, wherein the administered composition comprises one or more polypeptide fragment having a molecular weight of:

      a) less than 30,000 Da, or

      b) less than 30,000 Da and greater than or equal to 10,000 Da.

37. (withdrawn) The method of claim 35, wherein the administered composition comprises one or more polypeptide fragment having an amino acid length of less than 250 amino acids.

38. (withdrawn) The method of claim 35, wherein the administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 14 that is:

      a) at least 80%;

      b) at least 90%; or

      c) 100%.

39. (withdrawn and currently amended) The method of claim 35, wherein the composition comprises one or more polypeptide fragment selected from:

      (a) KSVSFSYKG (SEQ ID NO: 2);

      (b) QSVVFSYKG (SEQ ID NO:20)

      (c) KIMIGVERS (SEQ ID NO: 3);

      (d) ~~(c)~~ KLGNNVDFRI [SEQ ID NO: 4];

      (e) RIESLPIKPRG (SEQ ID NO: 5);

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(f) KHWSIWQIQDSSGKE (SEQ ID NO: 6);

(g) KNWNIWQIQDSSGKE (SEQ ID NO:21);

(h) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);

(i) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)

(j) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);

(k) RNLYPSGLPEEYSFLTTFRM (SEQ ID NO:23);

(l) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);

(m) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and

(n) RSSATLFVDCNRI [SEQ ID NO: 11).

(a) ~~K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];~~

(b) ~~KI/LMIG/SVER/TS/T [SEQ ID NO: 21];~~

(d) ~~R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];~~

(e) ~~KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23];~~

(f) ~~RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];~~

(g) ~~R/SH/N/AL/YPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];~~

(h) ~~FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26];and~~

(i) ~~R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].~~

40. (withdrawn and currently amended) The method of claim 35, wherein the composition comprises one or more polypeptide fragment selected from:

(a) KSVSFSYKG (SEQ ID NO: 2);

(b) QSVVFSYKG (SEQ ID NO:20)

(c) KIMIGVERS (SEQ ID NO: 3);

(d) RIESLPIKPRG (SEQ ID NO: 5);

(e) KHWSIWQIQDSSGKE (SEQ ID NO: 6);

(f) KNWNIWQIQDSSGKE (SEQ ID NO:21)

(g) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);

(h) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)

(i) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);

(j) RNLYPSGLPEEYSFLTTFRM (SEQ ID NO:23);

(k) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);

(l) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and

(m) RSSATLFVDCNRI [SEQ ID NO: 11).

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(a) ~~K/QSVS/VFSYKG [SEQ ID NO: 28]~~;

(b) ~~KIMIGVERTS [SEQ ID NO: 3, 10]~~;

(c) ~~RIESLPIKPRG [SEQ ID NO: 5]~~;

(d) ~~KH/NWS/NIWQIQDSGK [SEQ ID NO: 29]~~;

(e) ~~RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30]~~;

(f) ~~RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31]~~;

(g) ~~FSNLP/SSLFDSQWHKI [SEQ ID NO: 32]~~;

(h) ~~RSSATLFVDCNRI [SEQ ID NO: 11]~~.

41. (withdrawn) The method of claim 35, wherein the individual is a naive individual.

42. (withdrawn) The method of claim 35, wherein said administering treats or prevents a degenerative condition.

43. (withdrawn) The method of claim 42, wherein the degenerative condition or disease is arthritis or a musculoskeletal degenerative condition.

44. (withdrawn) The method of claim 43, wherein the degenerative condition or disease is rheumatoid arthritis, osteoarthritis, disc degeneration, or osteoporosis.

45. (withdrawn) The method of claim 42, wherein the administered composition comprises one or more polypeptide fragment having a molecular weight of:

      a) less than 30,000 Da, or

      b) less than 30,000 Da and greater than or equal to 10,000 Da.

46. (withdrawn) The method of claim 42, wherein the administered composition comprises one or more polypeptide fragment having an amino acid length of less than 250 amino acids.

47. (withdrawn) The method of claim 42, wherein the administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 14 that is:

      a) at least 80%;

      b) at least 90%; or

      c) 100%.

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48. (withdrawn and currently amended) The method of claim 42, wherein the composition
comprises one or more polypeptide fragment selected from:

> (a) KSVSFSYKG (SEQ ID NO: 2];
>
> (b) QSVVFSYKG (SEQ ID NO:20)
>
> (c) KIMIGVERS (SEQ ID NO: 3];
>
> (d) ~~(c)~~ KLGNNVDFRI [SEQ ID NO: 4];
>
> (e) RIESLPIKPRG (SEQ ID NO: 5];
>
> (f) KHWSIWQIQDSSGKE (SEQ ID NO: 6];
>
> (g) KNWNIWQIQDSSGKE (SEQ ID NO:21];
>
> (h) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7];
>
> (i) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22]
>
> (j) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8];
>
> (k) RNLYPSGLPEEYSFLTTFRM (SEQ ID NO:23];
>
> (l) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9];
>
> (m) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24]; and
>
> (n) RSSATLFVDCNRI [SEQ ID NO: 11].

> ~~(a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];~~
>
> ~~(b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21];~~
>
> ~~(d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];~~
>
> ~~(e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23];~~
>
> ~~(f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];~~
>
> ~~(g) R/SH/N/AL/TYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];~~
>
> ~~(h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26];and~~
>
> ~~(i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].~~

49. (withdrawn and currently amended) The method of claim 42, wherein the composition
comprises one or more polypeptide fragment selected from:

> (a) KSVSFSYKG (SEQ ID NO: 2];
>
> (b) QSVVFSYKG (SEQ ID NO:20]
>
> (c) KIMIGVERS (SEQ ID NO: 3];
>
> (d) RIESLPIKPRG (SEQ ID NO: 5];
>
> (e) KHWSIWQIQDSSGKE (SEQ ID NO: 6];

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(f) KNWNIWQIQDSSGKE (SEQ ID NO:21)

(g) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);

(h) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)

(i) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);

(j) RNLYPSGLPEEYSFLTTFRMT (SEQ ID NO:23);

(k) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);

(l) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and

(m) RSSATLFVDCNRI [SEQ ID NO: 11].

~~(a) K/QSVS/VFSYKG [SEQ ID NO: 28];~~

~~(b) KIMIGVERTS [SEQ ID NO: 3, 10];~~

~~(c) RIESLPIKPRG [SEQ ID NO: 5];~~

~~(d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];~~

~~(e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30];~~

~~(f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];~~

~~(g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32];~~

~~(h) RSSATLFVDCNRI [SEQ ID NO: 11].~~

50. (withdrawn) The method of claim 42, wherein the individual is a naive individual.

51. (withdrawn) A method for isolating a polypeptide fragment having anti-arthritic or anti-inflammatory activity comprising:

      (i)   incubating a connective tissue in a buffered autolysis medium to release a mixture of polypeptide fragments containing GAG polypeptide fragments and non-GAG polypeptide fragments;

      (ii)   fractionating the polypeptide fragments by size to produce a fraction of polypeptides fragments having a molecular weight of less than 30 KDa;

      (iii)   separating GAG-polypeptide fragments from non-GAG polypeptide fragments; and

      (iv)   recovering one or more non-GAG polypeptides fragment having a molecular weight less than 30 KDa, and having anti-arthritic or anti-inflammatory activity.

52. (withdrawn) The method of claim 51, wherein the autolysis medium has a pH range of:

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> a) about pH 2.5 to about pH 8.5;
>
> b) pH 3.5 to about pH 8;
>
> c) pH 4 to about pH 7; or
>
> d) pH 4.5 to about pH 7.

53. (withdrawn) The method of claim 35, wherein said administering treats or prevents an autoimmune response in the individual to at least one antigenic component of cartilage.

54. (withdrawn) The method of claim 53, wherein the administered composition comprises one or more polypeptide fragment having a molecular weight of:

> a) less than 30,000 Da, or
>
> b) less than 30,000 Da and greater than or equal to 10,000 Da.

55. (withdrawn) The method of claim 53, wherein the polypeptide fragment has an amino acid length of less than 250 amino acids.

56. (withdrawn) The method of claim 53, wherein the administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 14 that is:

> a) at least 80%;
>
> b) at least 90%; or
>
> c) 100%.

57. (withdrawn and currently amended) The method of claim 53, wherein the administered composition comprises one or more polypeptide fragment selected from:

> (a) KSVSFSYKG (SEQ ID NO: 2);
>
> (b) QSVVFSYKG (SEQ ID NO:20)
>
> (c) KIMIGVERS (SEQ ID NO: 3);
>
> (d) (c) KLGNNVDFRI [SEQ ID NO: 4];
>
> (e) RIESLPIKPRG (SEQ ID NO: 5);
>
> (f) KHWSIWQIQDSSGKE (SEQ ID NO: 6);
>
> (g) KNWNIWQIQDSSGKE (SEQ ID NO:21);
>
> (h) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);
>
> (i) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)
>
> (j) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);

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(k) RNLYPSGLPEEYSFLTTFRM (SEQ ID NO:23);

(l) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);

(m) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and

(n) RSSATLFVDCNRI [SEQ ID NO: 11).

~~(a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];~~

~~(b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21];~~

~~(d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];~~

~~(e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23];~~

~~(f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];~~

~~(g) R/SH/N/AL/TYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];~~

~~(h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26];and~~

~~(i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].~~

58. (withdrawn and currently amended) The method of claim 53, wherein the administered composition comprises one or more polypeptide fragment selected from:

(a) KSVSFSYKG (SEQ ID NO: 2);

(b) QSVVFSYKG (SEQ ID NO:20)

(c) KIMIGVERS (SEQ ID NO: 3);

(d) RIESLPIKPRG (SEQ ID NO: 5);

(e) KHWSIWQIQDSSGKE (SEQ ID NO: 6);

(f) KNWNIWQIQDSSGKE (SEQ ID NO:21)

(g) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);

(h) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)

(i) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);

(j) RNLYPSGLPEEYSFLTTFRMT (SEQ ID NO:23);

(k) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);

(l) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and

(m) RSSATLFVDCNRI [SEQ ID NO: 11].

~~(a) K/QSVS/VFSYKG [SEQ ID NO: 28];~~

~~(b) KIMIGVERTS [SEQ ID NO: 3, 10];~~

~~(c) RIESLPIKPRG [SEQ ID NO: 5];~~

~~(d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];~~

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~~(e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30];~~

~~(f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];~~

~~(g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32];~~

~~(h) RSSATLFVDCNRI [SEQ ID NO: 11].~~

59. (withdrawn) The method of claim 42, wherein said administering induces cartilage formation in the individual.

60. (withdrawn) The method of claim 59, wherein the administered composition comprises one or more polypeptide fragment having a molecular weight of:

        a) less than 30,000 Da, or

        b) less than 30,000 Da and greater than or equal to 10,000 Da.

61. (withdrawn) The method of claim 59, wherein the administered composition comprises one or more polypeptide fragment having an amino acid length of less than 250 amino acids.

62. (withdrawn) The method of claim 59, wherein the administered composition comprises one or more polypeptide fragment having identity to SEQ ID NO: 14 that is:

        a) at least 80%;

        b) at least 90%; or

        c) 100%.

63. (withdrawn and currently amended) The method of claim 59, wherein the composition comprises one or more polypeptide fragment selected from:

        (a) <u>KSVSFSYKG (SEQ ID NO: 2);</u>

        (b) <u>QSVVFSYKG (SEQ ID NO:20)</u>

        (c) <u>KIMIGVERS (SEQ ID NO: 3);</u>

        <u>(d)</u> (c) KLGNNVDFRI [SEQ ID NO: 4];

        (e) <u>RIESLPIKPRG (SEQ ID NO: 5);</u>

        (f) <u>KHWSIWQIQDSSGKE (SEQ ID NO: 6);</u>

        (g) <u>KNWNIWQIQDSSGKE (SEQ ID NO:21);</u>

        (h) <u>RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);</u>

        (i) <u>RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)</u>

        (j) <u>RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);</u>

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(k) RNLYPSGLPEEYSFLTTFRM (SEQ ID NO:23);

(l) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);

(m) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and

(n) RSSATLFVDCNRI [SEQ ID NO: 11].

(a) K/QSVS/V/A/EFSYKG [SEQ ID NO: 20];

(b) KI/LMIG/SVER/TS/T [SEQ ID NO: 21];

(d) R/KI/VES/TLP/NIKPR/KG [SEQ ID NO: 22];

(e) KH/N/YWS/N/TIWQIQDS/AGK/R [SEQ ID NO: 23];

(f) RIGQDDLPGFDLISQFQI/VD/EKA [SEQ ID NO: 24];

(g) R/SH/N/AL/TYPN/SGLPE/DEYSFLTTFR [SEQ ID NO: 25];

(h) FS/LN/HLP/SS/FLFDSQ/RWHKI/L [SEQ ID NO: 26];and

(i) R/TS/TSA/VTLFV/IDCN/IR/KI/V [SEQ ID NO: 27].

64. (withdrawn and currently amended) The method of claim 59, wherein the composition comprises one or more polypeptide fragment selected from:

(a) KSVSFSYKG (SEQ ID NO: 2);

(b) QSVVFSYKG (SEQ ID NO:20)

(c) KIMIGVERS (SEQ ID NO: 3);

(d) RIESLPIKPRG (SEQ ID NO: 5);

(e) KHWSIWQIQDSSGKE (SEQ ID NO: 6);

(f) KNWNIWQIQDSSGKE (SEQ ID NO:21)

(g) RIGQDDLPGFDLISQFQIDKA (SEQ ID NO: 7);

(h) RIGQDDLPGFDLISQFQVDKA(SEQ ID NO:22)

(i) RHLYPNGLPEEYSFLTTFRM (SEQ ID NO: 8);

(j) RNLYPSGLPEEYSFLTTFRMT (SEQ ID NO:23);

(k) KGLDGSLQTAAFSNLPSLFDSQWHKI (SEQ ID NO: 9);

(l) KGLDGSLQTAAFSNLSSLFDSQWHKI (SEQ ID NO:24); and

(m) RSSATLFVDCNRI [SEQ ID NO: 11].

(a) K/QSVS/VFSYKG [SEQ ID NO: 28];

(b) KIMIGVERTS [SEQ ID NO: 3, 10];

(c) RIESLPIKPRG [SEQ ID NO: 5];

(d) KH/NWS/NIWQIQDSGK [SEQ ID NO: 29];

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~~(e) RIGQDDLPGFDLISQFQI/VDKA [SEQ ID NO: 30];~~

~~(f) RH/NLYPN/SGLPEEYSFLTTFR [SEQ ID NO: 31];~~

~~(g) FSNLP/SSLFDSQWHKI [SEQ ID NO: 32];~~

~~(h) RSSATLFVDCNRI [SEQ ID NO: 11].~~

65. (cancelled)

66. (withdrawn) A method of treating or preventing in an individual an immune response to an
antigenic component of collagen, comprising:

administering to the individual an isolated polypeptide or fragment thereof, the
polypeptide having at least 65% identity to SEQ ID NO: 14;

wherein said administering induces tolerance to said at least one antigenic
component of collagen.

67. (new) The composition of claim 29, wherein the polypeptide comprises a fragment selected
from:

(a) residues 1-245 of SEQ ID NO:14;

(b) residues 6-245 of SEQ ID NO:14;

(c) residues 6-192 of SEQ ID NO:14;

(d) residues 6-186 of SEQ ID NO:14;

(e) residues 6-185 of SEQ ID NO:14;

(f) residues 6-73 of SEQ ID NO:14; and

(g) residues 85-185 of SEQ ID NO:14.